# Comparison of prepectoral and subpectoral breast reconstruction after mastectomies: A systematic review and meta analysis

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## ABSTRACT

Background: The safety of prepectoral breast reconstruction (PBR) after mastectomies as compared to subpectoral breast reconstruction (SBR) were unclear, so we conducted a systematic review to analyze their differences.
Methods: PubMed, EMBASE, the Cochrane Library, and Web of Science databases were searched to retrieve studies that compared PBR with SBR after mastectomies. The outcomes were complications, oncological safety, patient-reported outcomes and postoperative pain. Revman software version 5.30 and stata vesion 12 was used to conduct meta-analysis where possible.
Results: 16 comparative studies (12 articles and four abstracts) were included. The meta analysis showed no statistical differences in overall complications, implant loss, seroma, nipple or skin flap necrosis, hematoma, reoperation, wound dehiscence, and wound-skin infection, rippling between PBR and SBR. PBR might be associated with fewer nipple or skin flap necrosis for those who received tissue expander placement, and fewer capsular contracture rates for those who received implant. PBR might be associated with better Breast Q scores and less postoperative pain without increasing the risk of local recurrence and metastatic disease.
Conclusion: Although available evidence is limited, PBR might be as safe as subpectoral approach. Future well designed multicenter randomized controlled trial that compare postmastectomy PBR with SBR is needed.

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## Background

The development of mastectomy techniques, such as skin-sparing (SSM) and nipple-sparing approaches (NSM), conserved breast skin or the nipple-areola complex without increasing the local recurrence rates [1,2]. Postmastectomy breast reconstruction might improve the quality of life by extending the sense of sexuality, body image, and self-esteem with oncological safety and good cosmetic results [3–5]. The current standard, most common technique of breast reconstruction is to place prosthetic devices into the submuscular pocket behind the pectoralis major muscle (PMM), which could reduce implant visibility, palpability, and rippling [6–8]. This procedure needs to detach the PMM, and might result in muscle related complications (including injury-induced muscular deficit, muscle spasm, loss of strength), dissatisfaction about breast reconstruction (such as animation deformity, insufficient lower pole fullness, limited optimal placement of the device) and postoperative pain [5,7,9–12].

With the technical advancements, implant-based breast reconstruction (IBBR) could be finished without manipulation of the PMM as a prepectoral fashion [10]. Prepectoral breast reconstruction (PBR) was first reported in several decades ago with a high incidence of complications, including mastectomy skin flap necrosis, implant extrusion, and capsular contracture [13]. The introduction of the new materials, such as acellular dermal matrix (ADM) or titanium-coated poly propylene mesh (TCPM), could wrap the prosthesis entirely and place it underneath skin flaps safely [5,7,9]. This procedure was less invasive, challenging, time

consumed, and associated with reduced postoperative analgesics consumption, eliminated animation deformity, a more natural breast shape and less discomfort [4,9,10,14,15].

So we conducted a systematic review and meta-analysis to assess the outcomes (complications, oncological safety and cosmetic results) of PBR after mastectomies as compared to the standard breast reconstruction (SBR).

## Methods

### Search strategy

We searched PubMed, EMBASE, the Cochrane library, and Web of Science databases using mastectomies, mastectomy, prepectoral, subcutaneous, subpectoral, submuscular, retropectoral, breast reconstruction, tissue expander, implant, prothesis, prosthetic without language restrictions. We added subject heading terms in the searches if possible (Table S1). Reference lists from identified studies and relevant reviews were reviewed. Clinicaltrial.gov and meeting abstracts (Northeastern Society of Plastic Surgeons Annual Meeting) were searched to retrieve unpublished studies. Two reviewers (LL and JT) independently searched in September 2018 and updated in April 1, 2019.

### Inclusion criteria & study selection

We included studies that met the following criteria: patients receiving mastectomy (prophylactic and/or therapeutic mastectomy); interventions were PBR and SBR, no matter what kinds of prothesis. If the study compared prepectoral and subpectoral tissue expander (TE) or implant-based breast reconstruction (IBBR), it was also included. The outcomes were overall complications (implant loss, seroma, wound-skin infection, nipple or skin flap necrosis, hematoma, reoperation, wound dehiscence, capsular contracture), oncological safety (recurrence or metastasis), patient reported outcomes (Breast Q scores), and postoperative pain. The retrieved citations were screened by two reviewers (LL and JT) and inconsistencies were resolved by a third reviewer (JW).

### Data abstraction and quality assessment

The following information was abstracted by two reviewers (LL and JT) and checked by another two reviewers (YS and JW): author, publication year, age, follow-up, sample size, and inclusion criteria. If there were any disagreements, they were resolved by discussion. The quality of included studies were assessed using methodological index for non-randomized studies (MINORS) [16]. The "yes" item was scored "1", and the total score was calculated. If the total score was higher than 6, the overall study quality was regarded as moderate, and if the total score was higher than 9, the overall study quality was regarded as high.

### Data analysis

Revman software version 5.30 and stata software version 12 was used to conduct meta-analysis. Data was expressed using odds ratio (OR) and its 95% confidence interval (95%CI). $I^2$ test was used to analyze the percentage of variability across trials, which was deemed significant when I [2] was more than 40%. Data were pooled using fixed-effects model if I [2] < 40%, otherwise random model was used. Subgroup analysis was conducted to analyze the influence of prosthetic devices (TE vs. implant). Studies that did not specify the kinds of prosthetic devices were classified as "other". For IBBR, the influence of direct-to-implant (DTI) versus expander-implant (EI) technique was analyzed. Meta regression was used to explore the influence of study quality on the study effect. Meanwhile, cumulative meta-analysis was used to test the stability of the treatment effect. Publication bias was analyzed using funnel plot and Egger's test. It was thought to be significant when p-value was <0.05.

## Results

### Search results

165 citations were retrieved, and 111 citations were excluded based on titles and abstracts. 54 citations were screened based on full-text, 21 citations were not controlled studies, 8 studies were reviews or comments, 9 citations were not relevant. One study conducted by Zhu et al. used TE, so the data about TE was analyzed [17]. Finally, 12 articles [4,6,7,9,10,17—23] and four abstracts [24—27] were included for systematic review and 13 studies [4,6,7,9,10,17,19—24,27] were included for meta-analysis (Fig. S1).

### Characteristics of included studies

Four studies [6,9,18,21] were prospective studies, and others were retrospective studies. Two kinds of prosthetic coverage materials: ADM and TCPM, were used, and most used ADM. Six studies included patients with prophylactic and therapeutic mastectomy [6,7,10,18—20], and one study only included patients with therapeutic mastectomy [9]. Most studies (13/16) were regarded as moderate or high quality. Nearly all studies had clearly stated aims, inclusion of consecutive patients, contemporary groups, adequate control groups, appropriate endpoints, adequate statistical analyses, however, no studies prospectively calculated the study size and four studies collected data prospectively. Other details and quality of included studies were presented in Tables 1—2 and Table S2.

### Meta analysis

#### Surgery related complication

The meta-analysis showed no statistical significances in overall complications (OR 0.97, 95%CI 0.72 1.29) (Fig. 1), implant loss (OR 0.84, 95%CI 0.56 1.25) (Fig. 2), nipple or skin flap necrosis (OR 0.80, 95%CI 0.51 1.25) (Fig. 3), seroma (OR 0.88, 95%CI 0.53 1.47) (Fig. S2), wound-skin infection (OR 0.96, 95%CI 0.64 1.45) (Fig. S3), hematoma (OR 1.19, 95%CI 0.52 2.70) (Fig. S4), reoperation (OR 0.93, 95% CI 0.48 1.82) (Fig. S5) and wound dehiscence (OR 1.16, 95%CI 0.40 3.33) (Fig. S6). Fewer capsular contracture rates were found in prepectoral group than that in subpectoral group (OR 0.35, 95%CI 0.20 0.62) (Table 2, Fig. 4).

#### Subgroup analysis of TE and implant for surgery related complication

For those patients who underwent breast reconstruction with TE, the meta-analysis indicated no statistical significance in overall complications (OR 1.06, 95%CI 0.72 1.56) (Fig. 1), TE loss (OR 0.69, 95%CI 0.35 1.34) (Fig. 2), capsular contracture (OR 0.73, 95%CI 0.03 18.15) (Fig. 4), seroma (OR 0.66, 95%CI 0.34 1.30) (Fig. S2), wound-skin infection (OR 0.89, 95%CI 0.50 1.60) (Fig. S3), hematoma (OR 1.96, 95%CI 0.37 10.37) (Fig. S4), reoperation (OR 1.21, 95%CI 0.24 6.22) (Fig. S5), wound dehiscence (OR 0.81, 95%CI 0.04 17.41) (Fig. S6), and however, fewer nipple or skin flap necrosis events (OR 0.48, 95%CI 0.24 0.96) were found in prepectoral group than that in subpectoral group (Table 2, Fig. 3).

For those patients who underwent IBBR, the meta-analysis indicated no statistical significances in overall complications (OR 0.93, 95%CI 0.56 1.55) (Fig. 1), implant loss (OR 0.99, 95%CI 0.50

**Table 1**
Characteristics of included studies.

| Study | Country | Age | Study type | Stage | Prosthesis | Coverage prepectoral | Coverage subpectoral | Surgery | Outcomes | Follow-up (months) | Patients | Breast |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Baker 2018 | UK | 31–55 | P | Single | implant | ADM ± DSC | PMM + ADM | mastectomy | ①②③ | 3 | 28/12 | 43/19 |
| Bernini 2015 | Italy | 27–76 | P | Single | implant | TCPM | PMM + TCPM | SSM/NSM | ①③ | 16–42 | 39/34 | 34/29 |
| Bettinger 2017 | USA | 50.95 ± 11.83 | R | Two | TE-implant | ADM | PMM ± ADM | SSM/NSM/Modified radical | | 6m-6y | 110/103 | 165/129 |
| Cattelani 2017 | Italy | 26–75 | P | Single-/Two- | Implant/TE-implant | ADM | PMM | SSM/NSM | ②③ | 4–22 | 39/45 | 46/53 |
| Chandarana 2018 | UK | 51/50 | R | Single | implant | ADM | PMM + ADM | mastectomy | ① | 3 | 61/69 | 83/71 |
| Nahabedian 2017 | USA | 50.4/49.2 | R | Single-/Two- | TE-implant | ADM | PMM + ADM | SSM/NSM | ① | 21 | 39/50 | 62/63 |
| Sbitany 2017 | USA | 44.8/48.2 | P | Two | TE-implant | ADM | PMM + ADM | PMM + ADM | ① | 11.1–12.5 | 51/115 | 84/186 |
| Walia 2018 | USA | 51.4 ± 12.8/48.6 ± 9.1 | R | Two | TE | ADM | PMM + ADM | mastectomy | ①②③ | 2 | 26/109 | |
| Zhu 2016 | USA | 52.69 ± 12.18/50.48 ± 8.83 | R | Two | TE-Reconstruction Flaps | ADM | PMM + ADM | SSM/NSM | ①② | 2–34 | 29/59 | 50/108 |
| Sinnott2018 | USA | 52.4 ± 9.7/46.9 ± 8.8 | R | Single-/Two- | TE-implant | ADM | PMM + ADM | mastectomy | ① | 19.0 ± 16.9/31.9 ± 22.4 | 274/100 | 426/163 |
| Chopra 2016 | USA | 51.9 ± 14.1 | R | Single | implant | ADM | – | – | ① | 283 days | 13/25 | 20/41 |
| Schaeffer 2018 | USA | 50 (27-7)/50 (29-71) | R | Two- | TE | ADM | PMM + ADM | SSM/NSM | ① | 6 months | 24/48 | 45/90 |
| Copeland-Halperin 2019 | USA | 49 (43–57.25) | R | Single-/Two- | Implant/TE-implant | ADM | PMM + ADM | / | ①② | 12 months | 94/58 | / |
| Cox 2016 | USA | / | R | Single | implant | / | / | NSM | ① | 33.9 ± 25.8 | 10/10 | / |
| Kanesalingam 2017 | UK | / | R | Single | implant | sling/mesh | PMM + sling/mesh | / | | / | 22/22 | / |
| Myers 2018 | USA | / | R | Two- | TE | / | / | / | | / | 32/89 | 46/162 |

ADM: acellular dermal matrix; TCPM: titanium-coated poly propylene mesh; P: prospective comparative study; R: retrospective comparative study; TE: tissue expander; ①:postoperative complications; ②: postoperative pain; ③: BREAST-Q.
DSC: dermal sling coverage; PMM: pectoralis major muscle.

1.98) (Fig. 2), nipple or skin flap necrosis (OR 1.50, 95%CI 0.63 3.57) (Fig. 3), seroma (OR 2.41 95%CI 0.76 7.67) (Fig. S2), wound-skin infection (OR 0.67, 95%CI 0.30 1.50) (Fig. S3), hematoma (OR 1.77, 95%CI 0.58 5.45) (Fig. S4), reoperation (OR 0.99, 95%CI 0.46 2.11) (Fig. S5) and wound dehiscence (OR 1.73, 95%CI 0.38 7.76) (Fig. S6). Fewer capsular contracture rates were found in prepectoral group than that in subpectoral group (OR 0.16, 95%CI 0.05 0.53) (Table 2, Fig. 4).

*Subgroup analysis of DTI versus EI technique for IBBR for surgery related complication*

For EI technique, no statistical significances in overall complications (OR 1.55, 95%CI 0.44, 5.44), implant loss (OR 2.21, 95%CI 0.42, 11.67), seroma (OR 4.47, 95%CI 0.51, 38.93), wound-skin infection (OR 3.55, 95%CI 0.39, 32.26), and nipple or skin flap necrosis (OR 1.31, 95%CI 0.21, 7.97) were found between prepectoral and subpectoral group [19] (Supplemental Table 3).

For DTI technique, also no statistical significance in overall complications (OR 0.84, 95%CI 0.48, 1.47), implant loss (OR 0.82, 95%CI 0.38, 1.78), seroma (OR 1.69, 95%CI 0.41, 6.99), wound-skin infection (OR 0.46, 95%CI 0.18, 1.17), nipple or skin flap necrosis (OR 1.56, 95%CI 0.58, 4.20), wound dehiscence (OR 1.73, 95%CI 0.38, 7.76), hematoma (OR 1.77, 95%CI 0.58, 5.45) and reoperation (OR 1.00, 95%CI 0.47, 2.12) were found. Fewer capsular contracture rates were found in prepectoral group than that in subpectoral group (OR 0.16, 95%CI 0.05, 0.53) (Supplemental Table 4).

Cumulative meta-analysis confirmed the stability across studies (Figs. S7–S15). Meta regression for study quality indicated that the variations in study quality did not affect the pooled effect size (Table S5). The funnel plot was asymmetrical for overall complications and wound-skin infection, symmetrical for other outcomes (Figs. S16–20), however, the Egger's test (p > 0.05) indicated the absence of bias (Table S5).

*Oncological safety*

Sinnott et al. assessed the local recurrence and metastatic events between prepectoral (274 patients) and subpectoral group (100 patients) for 31.9 ± 22.4 months and 19.0 ± 16.9 months. The local recurrence rate was 1.4% in prepectoral group, and 5.4% in subpectoral group. And the metastatic event was 0.3% in prepectoral group, and none in subpectoral group [20]. Nahabedian et al. reported one removal secondary to recurrence among 43 patients who received SBR with a mean follow-up of 8.7 months (range, 3–21 months) [10]. No significant differences in local recurrence or metastatic disease were found between SBR and PBR in these two studies [10,20].

*Patient-reported outcomes*

Mean global scores in Breast Q at 3 months postoperatively were similar for both prepectoral and subpectoral groups (two studies, 175 patients) [4,6]. This was consistent with an unpublished study reported by Highton et al. [12], which showed no statistical significance between two groups. However, Cattelani et al. showed psychosocial well-being and satisfaction with outcome were statistically better in prepectoral group [18]. Sinnott et al. did not find significant difference in rippling between the two groups, with 0.5% rippling in prepectoral group and none in subpectoral group [20]. This was confirmed by Cox et al. and Bernini et al., which also

**Table 2**
Quality assessment of included studies.

| | A clearly stated aim | Inclusion of consecutive patients | Prospective collection of data | Endpoints appropriate to the aim of the study | Unbiased assessment of the study endpoint | Follow-up period appropriate to the aim of the study | Loss to follow up less than 5% | Prospective calculation of the study size | An adequate control group | Contemporary groups | Baseline equivalence of groups | Adequate statistical analyses | Overall quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Baker 2018 | yes | yes | yes | yes | unclear | no | yes | unclear | no | yes | yes | yes | 8 |
| Bernini 2015 | yes | yes | yes | yes | unclear | yes | yes | unclear | yes | yes | yes | yes | 10 |
| Bettinger 2017 | yes | yes | no | yes | unclear | yes | yes | unclear | yes | yes | no | yes | 8 |
| Cattelani 2017 | yes | yes | yes | yes | unclear | yes | yes | unclear | yes | yes | no | yes | 9 |
| Chandarana 2018 | yes | yes | no | yes | unclear | no | yes | unclear | yes | yes | yes | yes | 8 |
| Nahabedian 2017 | yes | yes | no | yes | unclear | yes | yes | unclear | yes | yes | no | yes | 8 |
| Sbitany 2017 | yes | yes | yes | yes | unclear | yes | yes | unclear | yes | yes | no | yes | 9 |
| Walia 2018 | yes | yes | no | yes | unclear | no | yes | unclear | yes | yes | no | yes | 7 |
| Zhu 2016 | yes | yes | no | yes | unclear | yes | yes | unclear | yes | yes | yes | yes | 9 |
| Sinnott2018 | yes | yes | no | yes | unclear | yes | yes | unclear | yes | yes | yes | yes | 9 |
| Schaeffer 2018 | yes | yes | no | yes | unclear | yes | yes | unclear | yes | yes | yes | no | 8 |
| Copeland-Halperin 2019 | yes | yes | yes | yes | unclear | yes | yes | no | yes | yes | yes | yes | 10 |
| Cox 2016 | yes | yes | no | yes | unclear | unclear | unclear | unclear | yes | yes | yes | yes | 7 |
| Chopra 2016 | yes | yes | no | yes | unclear | unclear | unclear | unclear | no | yes | yes | yes | 6 |
| Kanesalingam 2017 | yes | yes | no | yes | unclear | unclear | unclear | unclear | no | yes | yes | yes | 6 |
| Myers 2018 | yes | yes | no | yes | unclear | unclear | unclear | unclear | no | unclear | yes | yes | 5 |

showed similar results in breast rippling in each group [9,24]. Significantly more patients in the prepectoral group were either very dissatisfied or dissatisfied with the amount of rippling of the implant, who underwent DTI reconstructions [6].

*Postoperative pain*

The intensity of pain was significantly lower for prepectoral versus subpectoral group on postoperative 1 and 7 day [4,18], 30 day [4] and three months [22]. However, other studies showed no significant difference in pain scores between the prepectoral and subpectoral groups during the first 7 days [12] and 3 months [6]. And patients with subcutaneous TE experienced lower average pain scores compared to submuscular TE during their admission [17,26], but pain at discharge and at the first clinic visit were similar [17]. Copeland-Halperin et al. showed prepectoral group required 33% fewer days on opioid analgesic medication (P = 0.016) and were 66% less likely to require opioid prescription refills (P = 0.027)[23]. However, Myers et al. showed post-operative narcotic use in prepectoral group was 19.81 morphine equivalents compared to 27.12 morphine equivalents in subpectoral group (p = 0.05) [26]. This is consistent with study conducted by Kanesalingam et al., which found no difference in analgesia requirements [25].

**Discussion**

Mastectomy skin necrosis is a significant problem after breast reconstruction, and occurred in 8.1% of breasts after IBBR [28]. Skin necrosis is heavily dependent upon gentle tissue handling and preservation of blood supply of the skin flaps in addition to the impact of comorbidities and the thickness of mastectomy skin flaps [11]. For two stage procedure, a TE is placed at the time of mastectomy, to preserve the natural footprint of the breast, and then exchanged for a prosthetic implant once the skin envelope has been expanded to the desired volume [4]. The prepectoral TE placement for immediate breast reconstruction has several potential benefits, ranging from a faster tissue expansion, the ability to fill the TE with greater volumes, a reduction in postoperative pain, and fewer postoperative expansion visits [4]. Fast and early expansion also adds stress to the skin flap, resulting in higher skin necrosis rates, causing rippling and visible prosthesis [3,4]. However, our review showed fewer skin necrosis rates in prepectoral TE group, which might be because that the skin is draped gently over the prothestic coverage materials resulting in minimal stress from implant weight and gravity [11]. IBBR can be performed in one or two stages, although one stage breast reconstruction might be associated with higher risk of surgical complications, reoperation, and removal of implant than two-stage [29]. In this review, nipple or skin flap necrosis was similar in those who underwent one or two stage IBBR. A recent meta-analysis revealed ADM significantly increased risk of flap necrosis (RR 2.39; 95% CI: 1.8—3.16) [30]. However, we did not observe a difference between those who received ADM and TCPM.

Capsular contracture remains the most commonly reported complication and reason for reoperation [31]. We found fewer capsular contracture rates in prepectoral group than those in subpectoral group for patients who underwent IBBR. This might be due to significantly thinner capsule wall, complete ADM envelope and no mechanical stress over the implant [8,9,32]. Bachour et al. identified several variables that might increase the risk of capsular contracture: longer duration of follow-up, breast reconstructive surgery in patients with a history of breast cancer, subglandular implant placement, postoperative hematoma, and a textured implant surface [33]. Hallberg et al. indicated that ADM might not be associated with increased risk of capsular contraction (risk ratio
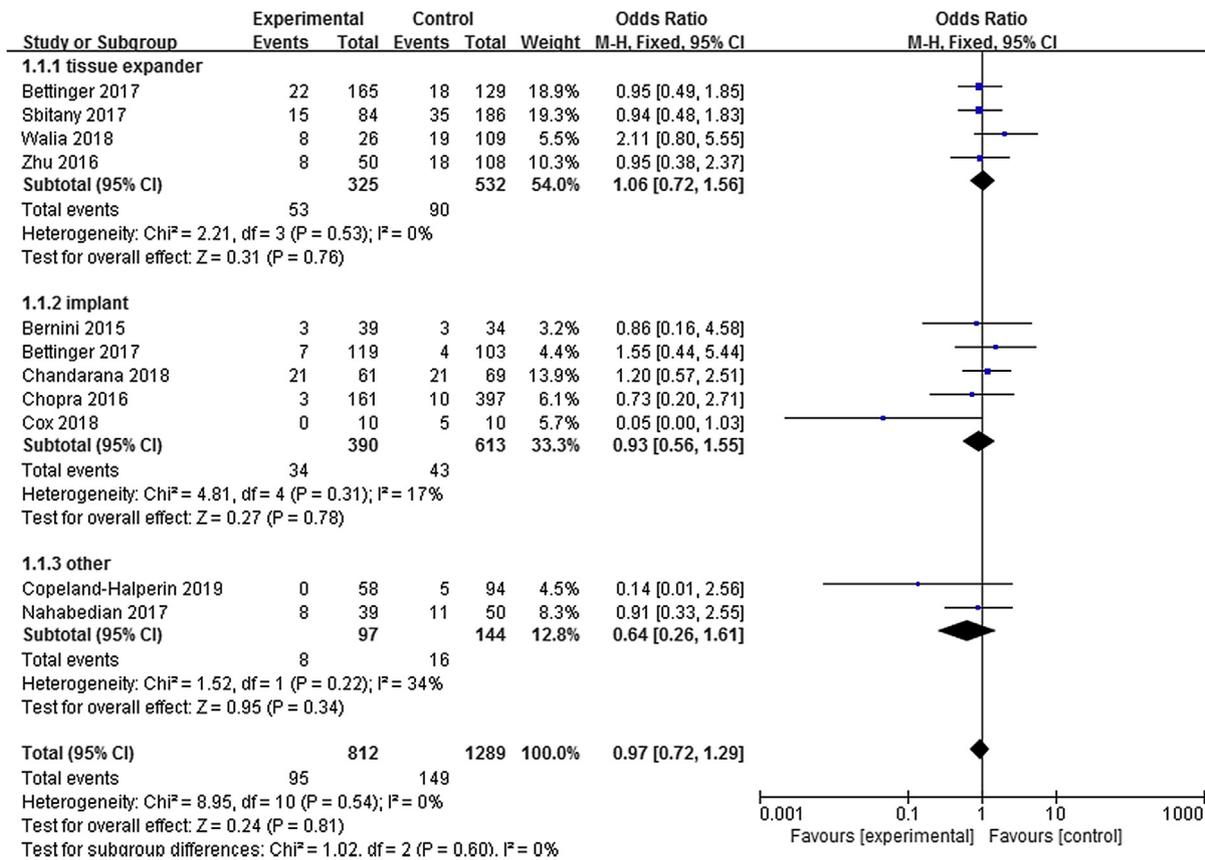
| Study or Subgroup | Experimental Events | Total | Control Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.1.1 tissue expander** | | | | | | | |
| Bettinger 2017 | 22 | 165 | 18 | 129 | 18.9% | 0.95 [0.49, 1.85] | |
| Sbitany 2017 | 15 | 84 | 35 | 186 | 19.3% | 0.94 [0.48, 1.83] | |
| Walia 2018 | 8 | 26 | 19 | 109 | 5.5% | 2.11 [0.80, 5.55] | |
| Zhu 2016 | 8 | 50 | 18 | 108 | 10.3% | 0.95 [0.38, 2.37] | |
| Subtotal (95% CI) | | 325 | | 532 | 54.0% | 1.06 [0.72, 1.56] | |
| Total events | 53 | | 90 | | | | |
| Heterogeneity: Chi² = 2.21, df = 3 (P = 0.53); I² = 0% | | | | | | | |
| Test for overall effect: Z = 0.31 (P = 0.76) | | | | | | | |
| | | | | | | | |
| **1.1.2 implant** | | | | | | | |
| Bernini 2015 | 3 | 39 | 3 | 34 | 3.2% | 0.86 [0.16, 4.58] | |
| Bettinger 2017 | 7 | 119 | 4 | 103 | 4.4% | 1.55 [0.44, 5.44] | |
| Chandarana 2018 | 21 | 61 | 21 | 69 | 13.9% | 1.20 [0.57, 2.51] | |
| Chopra 2016 | 3 | 161 | 10 | 397 | 6.1% | 0.73 [0.20, 2.71] | |
| Cox 2018 | 0 | 10 | 5 | 10 | 5.7% | 0.05 [0.00, 1.03] | |
| Subtotal (95% CI) | | 390 | | 613 | 33.3% | 0.93 [0.56, 1.55] | |
| Total events | 34 | | 43 | | | | |
| Heterogeneity: Chi² = 4.81, df = 4 (P = 0.31); I² = 17% | | | | | | | |
| Test for overall effect: Z = 0.27 (P = 0.78) | | | | | | | |
| | | | | | | | |
| **1.1.3 other** | | | | | | | |
| Copeland-Halperin 2019 | 0 | 58 | 5 | 94 | 4.5% | 0.14 [0.01, 2.56] | |
| Nahabedian 2017 | 8 | 39 | 11 | 50 | 8.3% | 0.91 [0.33, 2.55] | |
| Subtotal (95% CI) | | 97 | | 144 | 12.8% | 0.64 [0.26, 1.61] | |
| Total events | 8 | | 16 | | | | |
| Heterogeneity: Chi² = 1.52, df = 1 (P = 0.22); I² = 34% | | | | | | | |
| Test for overall effect: Z = 0.95 (P = 0.34) | | | | | | | |
| | | | | | | | |
| **Total (95% CI)** | | 812 | | 1289 | 100.0% | 0.97 [0.72, 1.29] | |
| Total events | 95 | | 149 | | | | |
| Heterogeneity: Chi² = 8.95, df = 10 (P = 0.54); I² = 0% | | | | | | | |
| Test for overall effect: Z = 0.24 (P = 0.81) | | | | | | | |
| Test for subgroup differences: Chi² = 1.02, df = 2 (P = 0.60), I² = 0% | | | | | | | |

0.001   0.1   1   10   1000
Favours [experimental]   Favours [control]

**Fig. 1.** The meta analysis results of overall complications.

0.55, 95%CI 0.38—1.69) [34]. Based on included studies, the incidence of capsular contraction between those who used ADM and TCPM were similar, which might indicate the choice of prosthetic coverage materials did not influence the development of capsular contracture. Adjuvant radiotherapy as a risk factor for developing capsular contracture in women after IBBR [35]. Magill et al. showed post-mastectomy radiation therapy was associated with significant increase in capsular contracture (7 studies, 2529 patients, OR 10.21, 95% CI 3.74 to 27.89) [36]. Sinnott et al. showed adjuvant radiotherapy might increase the rate of capsular contracture in the prepectoral group (16.1 vs 3.5%) and the subpectoral group (52.2 vs 2.9%) [20].

The PBR was considered when the mastectomy skin flaps were of adequate thickness and well perfused [10]. However, mastectomy skin thickness might not properly determine whether one should proceed with PBR or not. Obviously, thicker flaps are associated with improved vascularity and enhanced tissue support; however, thin flaps are at increased risk for delayed healing and mastectomy skin flap necrosis [10]. A recent consensus on nipple-sparing mastectomy indicated the risk of flap necrosis depends on the expertise and experience of the surgeon [37], which suggested skillful mastectomy technique might be crucial for the quality of mastectomy. Indeed, leaving "thicker" mastectomy skin flaps puts patients at unnecessary and unacceptable risk [12]. Sinnott et al. showed no significant differences in local recurrence or metastatic disease [20]. Putting a prosthetic device above PMM might influence the detection of local recurrence. Although the follow-up length was somewhat short, PBR was not associated with higher risk of local recurrence or metastatic events. From a reconstructive standpoint, well-perfused viable mastectomy skin flaps

are an absolute requirement, so skin perfusion should be assessed [11,14]. Jones et al. stated that ICG perfusion technology might be one of the available most accurate means for evaluating skin perfusion, by which they have been able to proceed with PBR in many patients with high-risk factors [11].

The quality of aesthetic outcomes for PBR has been excellent when compared with SBR. The surgeons' aesthetic outcome judgment is deemed excellent in 91% of prepectoral cases versus 65% of subpectoral cases, and this is coherent with the women subjective evaluation [9]. We found similar or better scores in Breast Q in prepectoral group as compared to subpectoral group. Casella et al. assessed 179 patients undergoing immediate PBR after mastectomy for 38.5 months and showed that significant higher rates in the BREAST-Q overall satisfaction, overall satisfaction with breasts, psychosocial and sexual well-being [38]. A significant concern with PBR is the development of traction rippling, particularly for individuals in whom the mastectomy skin flaps are naturally thin [12]. The absence of muscle coverage over the implant can expose the medial aspect of the reconstructed breast to more visible implant borders and signs of rippling, which can be corrected with multiple fat grafting rocedure over the implant capsule [9,20]. Bernini et al. [9] reported similar adjuvant lipofilling in each group, while Sinnott et al. [20] found the adjuvant lipofilling rate in subpectoral group is significantly higher than that in prepectoral group, which might be due to high proportion of postoperative radiation. Even though, significantly more patients in the prepectoral group were dissatisfied with the amount of rippling, who underwent a single-stage reconstruction [6]. It was said that the use of anatomic cohesive gel implants will be less prone to rippling and provide excellent shape approaching that of the natural breast
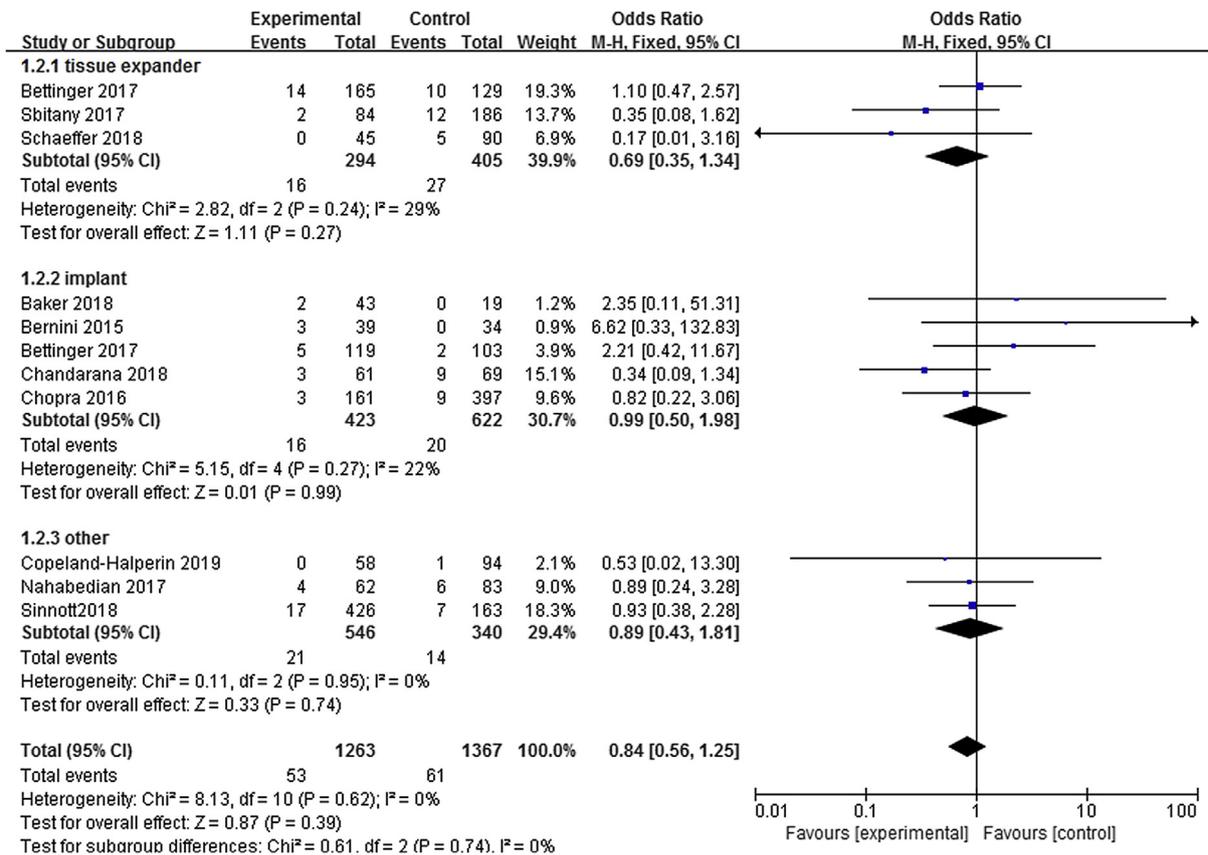
Fig. 2. The meta analysis results of implant loss.

in the second stage [11]. Downs et al. suggested capillary refill, thickness of flaps, presence of subcutaneous tissue, and temperature to touch are several variables that may be evaluated when considering whether to proceed with DTI [39]. PBR without manipulation of the PMM could avoid postoperative pain. Based on the included studies, similar or reduced postoperative pain was found.

What kinds of patients will be the ideal candidates for PBR? There is no consensus regarding to patient selection [40]. BMI was a factor that might influence the PBR outcomes, and some authors suggested the BMI should be less than 30 as BMI >30 might be associated with increased risk of complications [10,19,40]. Downs et al. suggested the BMI could range from 25 to 35[39]. However, low BMI (BMI<18.5) was also an exclusion criterion [9]. The breast volume was another consideration. Nahabedian et al. stated that the small-to-moderate breast volume might be the best [10,40]. Cattelani et al. suggested implant volume >550 mL should be not considered for PBR [18]. Patients with low degree of breast ptosis (grade 1 or 2) [12,18,39,40], nonsmoking [40], central breast tumors [40] should also be suitable for PBR. Large tumors or inflammatory breast carcinoma [8,19,41], positive lymph nodes or skin, or chest wall involvement [8,40,41] should be excluded for PBR due to a higher risk of chest wall recurrence and easier surveillance [8]. Patients with poorly controlled diabetes mellitus, tobacco use, immunocompromise, and previous radiation therapy might increase the incidences of complications, and further increase the reconstructive failures relative to ideal candidates [14,40]. Regarding to planned postmastectomy radiation therapy, several studies showed prepectoral IBBR in patients with postmastectomy radiation therapy show promising results and postmastectomy radiation therapy should not be an absolute contraindication to

prepectoral IBBR [20,42]. PBR has been shown to confer excellent cosmetic and functional outcomes in selected patients [43]. Careful patient selection is, however, critical for achieving successful outcomes as in the subpectoral approach [14]. In general, patients who have a normal BMI, small to medium breasts, and minimal co-morbidity, in addition to well-perfused mastectomy flaps, are the best candidates for the prepectoral approach [14].

*Strength and limitations*

Our study was the first one that compared PBR with SBR for breast cancer patients based on comprehensive search. However, our study has its own limitations: first: available studies were not randomized controlled trials (RCTs), they were prospectively or retrospectively comparative studies, the potential selective bias and imbalanced baselines of included patients might influence the study results. This means that the level of the evidence of the included studies is not high, indicating the need of further high quality studies. Second, MINORS was used for quality assessment and the results showed that the study quality varied. No studies calculated the sample size, and only four studies collected data prospectively. This further decreased the evidence level.

*Implications for future research and clinical practice*

PBR might be as safe as subpectoral approach with more benefits. A well designed multicenter RCT that compare prepectoral with subpectoral approach for postmastectomy breast reconstruction is needed due to limited and low evidence level. Wonderfully, we searched clincaltria.gov, and we found NCT02775409 has started to recruit patients which randomized patients to subcutaneous
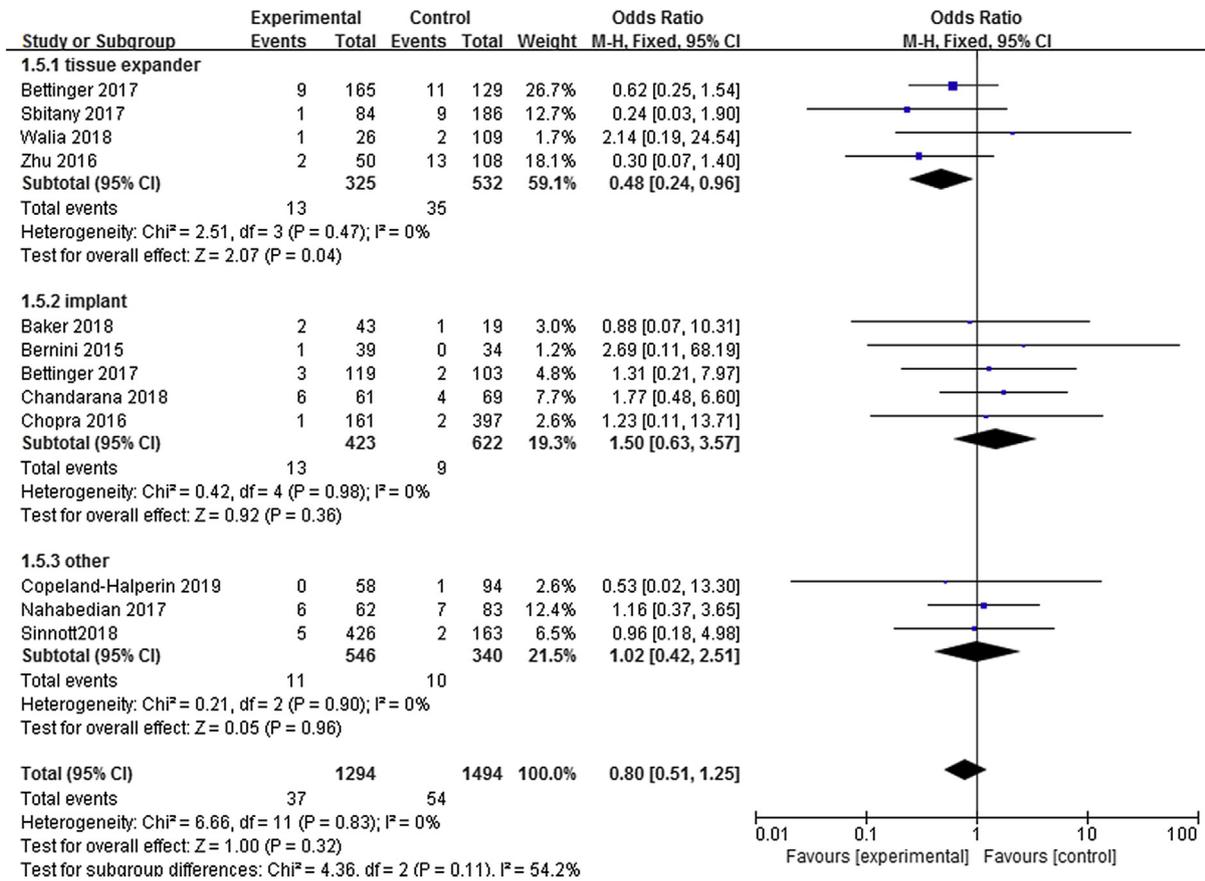
**Fig. 3.** The meta analysis results of nipple or skin flap necrosis.
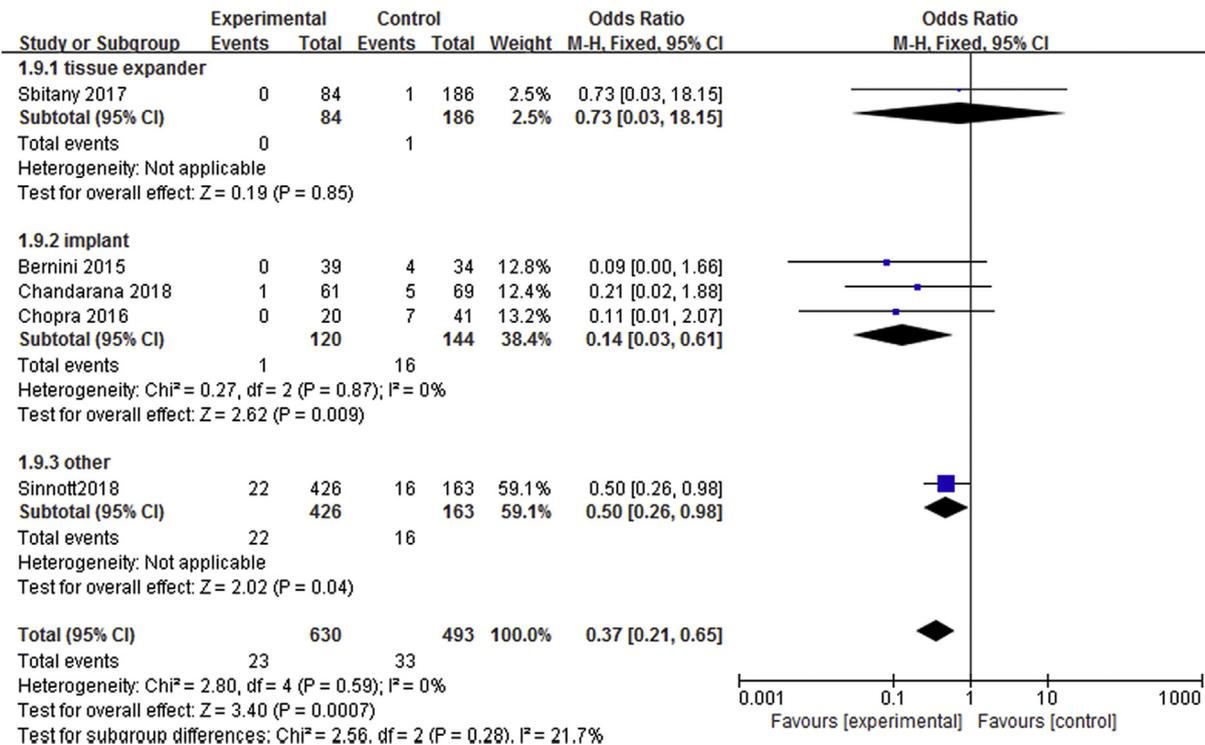


**Fig. 4.** The meta analysis results of capsular contracture.

or submuscular placement of TE group. This will help us to better figure out the benefits of prepectoral breast reconstruction. We found PBR by one stage was as safe as that by two stage, but no such a comparative study existed. Future studies should compare not only one step PBR with two step, but also PBR using ADM or TCPM. The follow-up of included studies were short for long-term complications, oncological safety and aesthetic outcomes assessment. In the future studies, these outcomes should be observed for a longer duration. For clinical practice, a careful patient selection and skin perfusion assessment should be conducted before PBR in order to reduce the complication rate and increase the oncological safety. In general, the best candidates for PBR might be those with normal BMI, small to medium breasts, and minimal comorbidity and well-perfused mastectomy flaps.

## Conclusion

We found that PBR might be as safe as subpectoral approach with more benefits. A well designed multicenter RCT that compare postmastectomy PBR with SBR with long-term follow-up is needed. For clinical practice, a comprehensive assessment of the patients should be well done in order to reduce the postoperative complications.

## Conflict of interest statement

None.

## Funding

## Author contribution

Study design: Lun Li, Jinhui Tian, Jiong Wu.
Literature search: Lun Li, Jinhui Tian.
Study selection: Lun Li, Jinhui Tian, Yonghui Su, Jiong Wu.
Data analysis: Lun Li, Jinhui Tian.
Manuscript writing: Lun Li, Yonghui Su, Xiaoyan Huang, Yingying Zhang, Jinhui Tian, Jia Wang, Jiangjing Hou, Weiru Chi, Bingqiu Xiu, Jiong Wu.
All authors reviewed the final manuscript and agreed to submit.

## Competing interests statement

All authors have no competing interests to declare.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.05.015.

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